Claims 15-17 are directed to kits as follows:

- 15. A kit, comprising:
- i) beads.
- ii) an insoluble support, and
- iii) conjugation means for linking nucleic acids to the beads and the beads to the support.
- 16. The kit of claim 15, wherein the solid support is selected from the group consisting of: beads, capillaries, plates, membranes, wafers, combs, pins, wafers with arrays of pits, and supports with nanoliter wells.
- 17. The kit of claim 15, wherein the bead is made from material selected from the group consisting of silica gel, glass, magnet, p-benzyloxybenzyl alcohol copolystyrene-divinyl benzene (DVB) resin, chlorotritylchloride copolystyrene-DVB resin, chloromethylated copolystyrene-DVB resin, metal, plastic, cellulose, cross-linked dextran, and agarose gel.

As noted in the previous response, particular basis for these claims may be found in the application as originally filed at page 7, lines 13-31, and page 13, lines 16-29, which recites:

In still another aspect, the invention provides a kit for immobilizing nucleic acids on beads, which are further bound to a solid support. In one embodiment, the kit comprises an appropriate amount of: i) beads, and/or ii) the insoluble support, and iii) conjugation means. The kits described herein can also optionally include appropriate buffers; containers for holding the reagents; and/or instructions for use.

This language is identical to the language of claim 15.

Support for claim 16 may be found, for example, in the specification at page 5, which describes alternative supports as follows:

Examples of insoluble supports for use in the instant invention include beads (silica gel, controlled pore glass, magnetic beads, Dynabeads, Wang resin; Merrifield resin, Sephadex/Sepharose beads, cellulose beads, etc.), capillaries, flat supports such as glass fiber filters, glass surfaces, metal surfaces (steel, gold silver, aluminum, silicon and copper), plastic materials including multiwell plates or membranes (e.g., of polyethylene, polypropylene, polyamide, polyvinylidenedifluoride), wafers, combs, pins or needles (e.g., arrays of pins suitable for combinatorial synthesis or analysis) or beads in an array of pits or nanoliter wells of flat surfaces such as wafers (e.g. silicon wafers), wafers with pits with or without filter bottoms.

Support for claim 17 may be found, for example, in original claim 2 and in the specification at page 6, which describes alternative bead materials as follows:

For example, the bead can be comprised of silica gel, glass (e.g. controlled-pore glass (CPG)), nylon, Wang resin, Merrifield resin, Sephadex, Sepharose, cellulose, magnetic beads, Dynabeads, a metal surface (e.g. steel, gold, silver, aluminum, silicon and copper), a plastic material (e.g., polyethylene, polypropylene, polyamide, polyester, polyvinylidenedifluoride (PVDF)) and the like. Beads can be swellable, e.g., polymeric beads such as Wang resin, or non-swellable (e.g., CPG).

Wang resin is p-benzyloxybenzyl alcohol copolystyrene-divinyl benzene (DVB) resin; Merrifield resin is chloromethylated copolystyrene-DVB resin, plastic, Sepharose is cross-linked dextran, and Sephadex is agarose gel.

Claims 18 and 19 find particular basis, for example, at page 6, which recites:

As used herein, the term "conjugated" refers to ionic or covalent attachment. Preferred conjugation means include: streptavidin- or avidinto biotin interaction; hydrophobic interaction; magnetic interaction (e.g. using functionalized Dynabeads); polar interactions, such as "wetting" associations between two polar surfaces or between oligo/polyethylene glycol; formation of a covalent bond, such as an amide bond, disulfide bond, thioether bond, or via crosslinking agents; and via an acid-labile linker. In a preferred embodiment for conjugating nucleic acids to beads, the conjugating means introduces a variable spacer between the beads and the nucleic acids. In another preferred embodiment, the conjugation is photocleavable (e.g. streptavidin- or avidin- to biotin interaction can be cleaved by a laser, for example for mass spectrometry).

Basis can also be found at page 10, which recites:

In certain embodiments, beads can be cross-linked to other beads, e.g., by use of homobifunctional crosslinking reagents. Cross-linked beads can provide additional mechanical strength compared to non-crosslinked beads.

Basis for claim 20, which recites that the nucleic acid molecule comprises protein nucleic acid, may be found, for example, at page 5, which recites:

Also included in the term "nucleic acid" are analogs of nucleic acids such as peptide nucleic acid (PNA), phosphorothioate DNA, and the like.

Basis for claim 21, which recites that the linkage is photocleavable, claim 22, which recites that the linkage is cleavable by exposure to a laser, and claim 23 may be found, for example, at page 5, which recites:

In another preferred embodiment, the conjugation is photocleavable (e.g. streptavidin- or avidin- to biotin interaction can be cleaved by a laser, for example for mass spectrometry).

Basis for claim 24 may be found, for example, at page 5, which recites that conjugation is effected through ionic linkages, may be found for example at page 6, which recites "[a]s used herein, the term "conjugated" refers to ionic or covalent attachment." Basis may also be found, for example, at page 8, which recites:

As pointed out above, the bead can also be associated with the solid support by non-covalent interactions. For example, a magnetic bead (e.g., a bead capable of being magnetized, e.g., a ferromagnetic bead) can be attracted to a magnetic solid support, and can be released from the support by removal of the magnetic field. Alternatively, the bead can be provided with an ionic or hydrophobic moiety, which can associate with, respectively, an ionic or hydrophobic moiety of the solid support.

Therefore, no new matter has been added.

INFORMATION DISCLOSURE STATEMENTS

37 C.F.R. §1.132 requires:

Any information disclosure statement filed under Section 1.97 shall include:

A list of all patents, publications, or other information submitted for consideration by the Office;



A legible copy of:

Each U.S. and foreign patent; Each publication or that portion which caused it to be listed; and

All other information or that portion which caused it to be listed, except that no copy of a U.S. patent application need be included; and

A concise explanation of the relevance, as it is presently understood by the individual designated in Section 1.56(c) most knowledgeable about the content of the information, of each patent, publication, or other information listed that is <u>not in the English</u> language. The concise explanation <u>may be either</u> separate from the specification or <u>incorporated</u> therein.

A copy of any patent, publication or other information listed in an information disclosure statement is not required to be provided if it was previously cited by or submitted to the Office in a prior application, provided that the prior application is properly identified in the statement and relied upon for an earlier filing date under 35 U.S.C. 120.

In this instance, applicant has complied with all of the above requirements. PTOL-1449 forms listing all patents, publications, or other information submitted for consideration by the Office have been provided; copies of the references have been provided or were provided in the parent application that is properly identified in the statement and relied upon for an earlier filing date under 35 U.S.C. 120. All, except for about five or six of the submitted documents are in the English; for those not in English, an English language abstract is provided that describes the subject matter of the document.

There is no requirement in 37 C.F.R. §§1.98-1.99 or 1.56 for a statement of relevance of any documents that are in the English language, nor is there a requirement to identify the ten most relevant references.

Therefore, consideration and entry of the Information Disclosure

Statements filed in connection with this application are respectfully requested.

Furthermore, it is not possible for the instant applicant to assess, which references the Office would deem most relevant. Applicant does not in any

manner want to mislead the Office nor in any manner compromise fulfillment of the duty of candor imposed by 37 C.F.R. §1.56.

It is noted that a copy of the Search Report from the International Searching Authority in connection with PCT International Patent Application No. PCT/US97/20194, which claims priority from U.S. Application Serial No. 08/746,036 was provided in the parent application. Copies of the cited documents were provided in the parent application and are also of record in the instant application. A copy of the Search Report is attached hereto. It is also noted that, with one exception based on a minor language issue, the claims were deemed novel and inventive over these references in the International Preliminary Examination Report.

CHANGE IN INVENTORSHIP

As noted in the previous response, upon review of the claims in this application, it was noticed that inventorship for the application was incorrect as filed. A Petition under 37 C.F.R. §1.48(a) to removed Dirk Reuter and G. Scott Higgins as inventors was filed in the previous response. Also provided were:

- (a) statements signed by Dr. Reuter and Dr. Higgins (a facsimile copy) indicating that the error in inventorship in the above-referenced application occurred without deceptive intent on the part of each;
- (b) an oath and declaration signed by the actual inventors;
- (c) a check including the fee set forth in 37 C.F.R. §1.17(i) (\$130.00);
- (d) written consent of Sequenom Inc., assignee of the entire title, right and interest in the above-captioned application; and
- (e) a Certificate under 37 C.F.R. §3.73(b) establishing ownership of the instant application by Sequenom Inc (with a copy of the assignment).

Acknowledgement of the change in inventorship is respectfully requested.

* * *

In view of the above remarks and the amendments and remarks of record, consideration and allowance of the application are respectfully requested.

Respectfully submitted, HELLER EHRMAN WHITE & McAULIFFE

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